

**Amendments to the Claims:**

This claim listing will replace all prior versions and listings of claims in the application:

**Claim Listing:**

1. (Currently Amended) A method for identifying a compound that inhibits senescence-associated changes in cellular gene expression in a mammalian cell, the method comprising the steps of:
  - (a) treating the mammalian cell in the presence and absence of the compound with an agent that induces senescence or culturing the mammalian cell in the presence and absence of the compound under conditions that induce senescence;
  - (b) assaying the mammalian cell for ~~repression or~~ induction of a cellular gene that is ~~repressed or~~ induced by p21 gene expression; and
  - (c) identifying the compound as an inhibitor of senescence-associated changes in cellular gene expression if ~~the gene that is repressed by p21 is repressed to a lesser extent, or~~ the gene that is induced by p21 is induced to a lesser extent, in the presence of the compound than in the absence of the compound.
2. (Original) The method of claim 1, wherein the mammalian cell is assayed for a cellular gene that is induced by p21.
3. (Original) The method of claim 2, wherein the gene is Fibronectin 1 (Acc. No. X02761), Plasminogen activator inhibitor, type I (Acc. No. M14083), Plasminogen activator, tissue type (Acc. No. M15518), Laminin  $\beta 2$  (Acc. No. X79683), Desmocollin 2a/bb (Acc. No. X56807), Podocalyxin-like protein (Acc. No. U97519), Activin A (inhibin  $\beta A$ ) (Acc. No. J03634), Galectin 3 (Mac-2) (Acc. No. AB006780), Mac-2 binding protein (Acc. No. L13210), Prosaposin (Acc. No. J03077), CTGF (connective tissue growth factor) (Acc. No. M92934), Granulin/epithelin (Acc. No. AF055008), Cathepsin B (Acc. No. L04288), Tissue transglutaminase (Acc. No. M55153), P37NB (slit homolog) (Acc. No. U32907), Serum amyloid A protein precursor (Acc. No. M26152), Alzheimer's disease amyloid A4 protein precursor (Acc. No. D87675), Complement C3 precursor (Acc. No. K02765), Testican (Acc. No. X73608), Integrin  $\beta 3$  (Acc. No. M35999), N-acetylgalactosamine-6-

sulfate sulfatase (Acc. No. U06088), Acid alpha-glucosidase (Acc. No. X55079), Acid lipase A (cholesterol esterase) (Acc. No. X76488), Lysosomal pepstatin-insensitive protease (CLN2) (Acc. No. AF017456), Superoxide dismutase 2 (Acc. No. X07834), Metaxin (Acc. No. J03060), 2,4-dienoyl-CoA reductase (Acc. No. U78302), Ubiquitin-conjugating enzyme (UbcH8) (Acc. No. AF031141), Ubiquitin-specific protease 8 (Acc. No. D29956), RTP/Cap43/Drg1/Ndr1 (Inducible by nickel, retinoids, homocysteine and ER stress) (Acc. No. D87953), C-193 muscle ankyrin-repeat nuclear protein (cytokine-inducible) (Acc. No. X83703), LRP major vault protein associated with multidrug resistance (Acc. No. X79882),  $\beta$ -arrestin related HHCPA78 homolog (upregulated by vitamin D3) (Acc. No. S73591), R-RAS (Acc. No. M14949), RAB 13 small GTPase (Acc. No. X75593), P66 SHC (ski oncogene) (Acc. No. U73377), MK-STYX (MAP kinase phosphatase-like protein) (Acc. No. N75168), H73 nuclear antigen/MA-3 apoptosis-related/TIS (topoisomerase-inhibitor suppressed) (Acc. No. U96628), Natural killer cells protein 4 (Acc. No. M59807), TXK tyrosine kinase (T-cell specific) (Acc. No. L27071), X-linked PEST-containing transporter (Acc. No. U05321), AMP deaminase 2 (Acc. No. M91029), FIP2/HYPL huntingtin-interacting protein (Acc. No. AF061034), DNASE I homolog (Acc. No. X90392), Transcription factor 11 (Acc. No. X77366), Histone H2A.2 (Acc. No. L19779), Histone H2B (Acc. No. AL021807), 23808 (Acc. No. AF038192), CGI-147 (Acc. No. AA307912), EST (Acc. No. W89120), EST (Acc. No. AI026140), EST (Acc. No. AA218982), or EST (Acc. No. W63684).

4. (Canceled)
5. (Canceled)
6. (Original) The method of claim 1, wherein expression of the cellular gene is detected using an immunological reagent.
7. (Original) The method of claim 1, wherein expression of the cellular gene is detected by assaying for an activity of the cellular gene product.
8. (Original) The method of claim 1, wherein expression of the cellular gene is detected by hybridization to a complementary nucleic acid.
- 9.-25. (Canceled)

26. (Newly added) A method for identifying a compound that promotes senescence-associated changes in cellular gene expression in a mammalian cell, the method comprising the steps of:
- (a) treating the mammalian cell with an agent that induces senescence in the presence or absence of the compound or culturing the mammalian cell under conditions that induce senescence in the presence and absence of the compound;
  - (b) assaying the mammalian cell for repression of induction of a cellular gene that is repressed or induced by p21 gene expression; and
  - (c) identifying a compound that promotes senescence-associated changes in cellular gene expression of a gene that is repressed by p21 is repressed in the presence of the compound, or a gene that is induced by p21 is induced in the presence of the compound.
27. (Newly added) The method of claim 26, wherein the mammalian cell is assayed for a cellular gene that is induced by p21.
28. (Newly added) The method of claim 27, wherein the gene is Fibronectin 1 (Acc. No. X02761), Plasminogen activator inhibitor, type I (Acc. No. M14083), Plasminogen activator, tissue type (Acc. No. M15518) Laminin  $\beta$ 2 (Acc. No. X79683), Desmocollin 2a/bb (Acc. No. X56807), Podocalyxin-like protein (Acc. No. U97519), Activin A (Inhibin  $\beta$ A) (Acc. No. J03634), Galectin 3 (Mac-2) (Acc. No. AB006780), Mac-2 Binding protein (Acc. No. L13210), Prosaposin (Acc. No. J03077), CTGF (connective tissue growth factor) (Acc. No. M92934), Grnulin/epithelin (Acc. No. AF055008), Cathepsin B (Acc. No. L04288), Tissue transglutaminase (Acc. No. M55153), P37NB (slit homolog) (Acc. No. U32907), Serum amyloid A protein precursor (Acc. No. M26152), Alzheimer's disease amyloid A4 protein precursor (Acc. No. D87675), Complement C3 precursor (Acc. No. K02765), Testican (Acc. No. X73608), Integrin  $\beta$ 3 (Acc. No. M35999), N-acetylgalactosamine-6-sulfate sulfatase (Acc. No. U06088), Acid alpha-glucosidase (Acc. No. X55079), Acid lipase A (cholesterol esterase) (Acc. No. X76488), Lysosomal pepstatin-insensitive protease (CLN2) (Acc. No. AF017456), Superoxide dismutase 2 (Acc. No. X07834), Metaxin (Acc. No.

J03060), 2,4-dienoyl-CoA reductase (Acc. No. U78302), Ubiquitin-conjugating enzyme (UbcH8) (Acc. No. AF031141), Ubiquitin-specific protease 8 (Acc. No. D29956), TRP/Cap43/Drgl/Ndrl (Inducible by nickel, retinoids, homocysteine and ER stress) (Acc. No. D87953), C-193 muscle ankyrin-repeat nuclear protein (cytokine-inducible) (Acc. No. X83703), LRP major vault protein associated with Multidrug resistance (Acc. No. X79882),  $\beta$ -arrestin related HHCPA78 homolog (upregulated by vitamin D3) (Acc. No. S73591), R-RAS (Acc. No. M14949), RAB 13 small GTPase (Acc. No. X75593), P66SHC (ski Oncogene) (Acc. No. U72277), MK-STYX (MAP kinase phosphatase-like protein) (Acc. No. N75168), H73 nuclear antigen/MA-3 apoptosis-related/TIS (topoisomerase-inhibitor suppressed) (Acc. No. U96628), Natural killer cells protein 4 (Acc. No. M59807), TXK tyrosine kinase (T-cell specific) (Acc. No. L27071), X-linked PEST-containing transporter (Acc. No. U-05321), AMP deaminase 2 (Acc. No. M91029), FIP2/HYPL huntingtin-interacting protein (Acc. No. AF061034), DNASE I homolog (Acc. No. X90392), Transcription factor 11 (Acc. No. X77366), Histone H2A.2 (Acc. No. L19779), Histone H2B (Acc. No. AL021807), 23808 (Acc. No. AF038192), CGI-147 (Acc. No. AA307912), EST (Acc. No. AI026140), EST (Acc. No. AA218982), or EST (Acc. No. W63684).

29. (Newly added)The method of claim 26, wherein expression of the cellular gene is detected using an immunological reagent.
30. (Newly added)The method of claim 26, wherein expression of the cellular gene is detected by assaying for an activity of the cellular gene product.
31. (Newly added)The method of claim 26, where expression of the cellular gene is detected by hybridization to a complementary nucleic acid.

32. (Newly added) A method of identifying a compound that induces senescence-associated changes in cellular gene expression in a mammalian cell, the method comprising the steps of:
- (a) assaying a mammalian cell in the presence and absence of the compound for expression of a gene whose expression is modulated by p21; and
  - (b) identifying a compound that induces senescence-associated changes in cellular gene expression if expression of a gene that is repressed by p21 is repressed in the cell, or expression of a gene that is induced by p21 is increased in the cell, to a greater extent in the presence than in the absence of the compound.
33. (Newly added) The method of claim 32, wherein the mammalian cell is assayed for a cellular gene that is induced by p21.
34. (Newly added) The method of claim 33, wherein the gene is Fibronectin 1 (Acc. No. X02761), Plasminogen activator inhibitor, type I (Acc. No. M14083), Plasminogen activator, tissue type (Acc. No. M15518) Laminin B2 (Acc. No. X79683), Desmocollin 2a/bb (Acc. No. X56807), Podocalyxin-like protein (Acc. No. U97519), Activin A (Inhibin B) (Acc. No. J03634), Galectin 3 (Mac-2) (Acc. No. AB006780), Mac-2 Binding protein (Acc. No. L13210), Prosaposin (Acc. No. J03077), CTGF (connective tissue growth factor) (Acc. No. M92934), Granulin/epithelin (Acc. No. AF055008), Cathepsin B (Acc. No. L04288), Tissue transglutaminase (Acc. No. M55153), P37NB (slit homolog) (Acc. No. U32907), Serum amyloid A protein precursor (Acc. No. M26152), Alzheimer's disease amyloid A4 protein precursor (Acc. No. D87675), Complement C3 precursor (Acc. No. K02765), Testican (Acc. No. X73608), Integrin B3 (Acc. No. M35999), N-acetylgalactosamine-6-sulfate sulfatase (Acc. No. U06088), Acid alpha-glucosidase (Acc. No. X55079), Acid lipase A (cholesterol esterase) (Acc. No. X76488), Lysosomal pepstatin-insensitive protease (CLN2) (Acc. No. AF017456), Superoxide dismutase 2 (Acc. No. X07834), Metaxin (Acc. No. J03060), 2,4-dienoyl-CoA reductase (Acc. No. U78302), Ubiquitin-conjugating enzyme (UbcH8) (Acc. No. AF031141), Ubiquitin-specific protease 8 (Acc. No. D29956), TRP/Cap43/Drg1/Ndr1 (Inducible by nickel, retinoids, homocysteine

and ER stress) (Acc. No. D87953), C-193 muscle ankyrin-repeat nuclear protein (cytokine-inducible) (Acc. No. X83703), LRP major vault protein associated with Multidrug resistance (Acc. No. X79882),  $\beta$ -arrestin related HHCPA78 homolog (upregulated by vitamin D3) (Acc. No. S73591), R-RAS (Acc. No. M14949), RAB 13 small GTPase (Acc. No. X75593), P66SHC (ski Oncogene) (Acc. No. U72277), MK-STYX (MAP kinase phosphatase-like protein) (Acc. No. N75168), H73 nuclear antigen/MA-3 apoptosis-related/TIS (topoisomerase-inhibitor suppressed) (Acc. No. U96628), Natural killer cells protein 4 (Acc. No. M59807), TXK tyrosine kinase (T-cell specific) (Acc. No. L27071), X-linked PEST-containing transporter (Acc. No. U-05321), AMP deaminase 2 (Acc. No. M91029), FIP2/HYPL huntingtin-interacting protein (Acc. No. AF061034), DNASE I homolog (Acc. No. X90392), Transcription factor 11 (Acc. No. X77366), Histone H2A.2 (Acc. No. L19779), Histone H2B (Acc. No. AL021807), 23808 (Acc. No. AF038192), CGI-147 (Acc. No. AA307912), EST (Acc. No. AI026140), EST (Acc. No. AA218982), or EST (Acc. No. W63684).

35. (Newly added)The method of claim 32, wherein expression of the gene is detected using an immunological reagent.
36. (Newly added)The method of claim 32, wherein expression of the gene is detected by assaying for an activity of the cellular gene product.
37. (Newly added)The method of claim 32, where expression of the gene is detected by hybridization to a complementary nucleic acid.
38. (Newly added)The method of claim 32, wherein the mammalian cell comprises an inducible p21 gene, and wherein the assay is subpart (a) is performed in the presence of an amount of an agent that induced p21 expression whereby the extent of p21 induction is insufficient for complete inhibition of genes inhibited by p21.